Expanding Access to Movement Disorders Care and Research

Disclosures

- Presbyterian Home of Central New York
- Susquehanna Nursing and Rehabilitation Center
- Samaritan Keep Nursing Home
- Otsego Focus Nursing and Rehabilitation Center
- Sitrin Nursing Home
- Greater Rochester Health Foundation
- AMC Health
- NINDS
Outline

• Access to neurological care is vital but limited
• Telemedicine facilitates access to care
• Technology can improve clinical research
The burden of chronic conditions such as Parkinson disease is growing globally

Distribution of individuals with Parkinson disease by country from 2005 to 2030*

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>100%</td>
<td>China, 48%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brazil, 4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>U.S., 8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>India, 8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Europe, 20%</td>
</tr>
<tr>
<td>2030</td>
<td>100%</td>
<td>China, 57%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brazil, 4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>U.S., 7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>India, 8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Europe, 14%</td>
</tr>
<tr>
<td></td>
<td>Others, 10%</td>
<td></td>
</tr>
</tbody>
</table>

*Among individuals over 50 in the world’s ten most and Western Europe’s five most populous nations

Source: Neurology 2007;68:384-6

Increased access to specialists can improve care and outcomes

Model of improving outcomes

- Increased/improved access to specialists
  - Specialists lead to higher quality care
    - Heart disease → More appropriate medication use
    - Asthma → Greater adherence to national management guidelines
    - Diabetes → Better process measures
  - Higher quality care improves outcomes
    - Heart failure → Increased survival
    - Asthma → Improved quality of life
    - Diabetes → Fewer complications

In Parkinson disease, movement disorder specialist involvement is associated with higher adherence to quality indicators than general neurologist or other specialty involvement

Access to Neurologist Care is Vital

Neurologist Care in PD
- 14% reduction in hip fracture
- 21% reduction in SNF
- 22% less likely to die

A.W. Willis et al. Neurology 2011;77:851-857

Access to neurological care is limited in the United States

Proportion of Medicare beneficiaries with PD who do not see a neurologist

Percentage without Neurologist Care
- 0 – 23%
- 24 – 52%
- 53 – 76%
- 77 – 100%

Outline

- Access to neurological care is vital but limited

  - Telemedicine facilitates access to care
    - Technology can improve clinical research
    - Vision for movement disorders in South Florida

Simple, inexpensive technology can reach patients with PD wherever they live
Novel application of existing technology

Equipment
- Internet-enabled device
- Web cam, microphone
- Encrypted software

- In-home care
- Remote patient monitoring
- Remote study participation
University of Rochester Telemedicine Network of Upstate New York
A spoke and hub model providing care to communities through regional nursing homes

We conducted a pilot, randomized controlled study to evaluate the feasibility of a spoke and hub model

Pilot randomized, controlled study of telemedicine for Parkinson disease

Outcomes
Primary outcome
- Feasibility as measured by proportion of telemedicine visits completed as scheduled

Secondary outcomes
- Reliability and validity of the UPDRS motor examination
- Quality of life
- Patient satisfaction
- Motor performance
- Mood
- Cognition

Telemedicine visits were feasible
Remote assessment of the UPDRS was reliable
QOL, satisfaction with care and motor function improved

This model increases access to individuals residing in rural communities

More importantly, patients were touched ...
... and moved by the experience

The same model can be extended into the home...

“Virtual House calls”
A randomized controlled trial of virtual house calls for PD

20 patients with PD at two centers
- 11 patients receive 3 in-person visits over 6 months
- 9 patients receive 3 telemedicine visits over 6 months in home

Outcomes
1. Feasibility
2. Clinical outcomes
3. Economic value

Average distance from UR Movement disorders Clinic
55.8 miles and average drive time of 64.7 minutes

Sponsors:

Virtual house calls flip the care paradigm
Patient time spent on in-person versus telemedicine visits

We have completed a national randomized controlled trial of telemedicine for Parkinson disease

In collaboration with:

Source: Teledermatology and e-Health. February 2016 (ePub ahead of print)

**PRELIMINARY RESULTS**

**Feasibility**
98% of individuals completed at least one telemedicine visit.
91% of 388 telemedicine visits completed as scheduled.

**Effectiveness**
No difference in PDQ39 (QOL, 0-100);
95% CI -2.0 to 2.7, p=0.78
Both groups improved in PACIC (quality of care, 0-5) but no difference between groups; 95% CI -0.21 to 0.28, p=0.79

**Value**
Median of 80 minutes and 108 miles per visit saved in telemedicine group. Despite this there was no difference in caregiver strain.
Patients and Physicians were satisfied with the telemedicine visits

Selected patient feedback
- "I learned more in one visit than all the information provided by other physicians over a period of years!!"
- "I felt it was a great doctor’s visit. Better than many I’ve had face to face."
- "It was so good to not have to ride 45 minutes in a handicapped van each way to see a (movement disorder specialist)."

Selected physician feedback
- "Visit interaction was great, but it was very difficult to determine actual ratings for rapidly alternating movements."
- "Video quality, particularly for rating Unified Parkinson’s Disease Rating Scale is frustrating."
- "I think it is fine for the interview part, and maybe for clinical follow-ups."

We are launching PDCNY to enable any New Yorker with PD to receive multidisciplinary care in the home

Supporting Information
- Approximately 7000 patients with PD and 4000 with limited access to neurological care

Source: Telemedicine and e-Health. February 2016 (ePub ahead of print)
Outline

- Access to neurological care is vital but limited
- Telemedicine facilitates access to care
- Technology can improve clinical research

The productivity of the drug development industry continues to decline

New molecular entities per $1 billion in R&D (inflation adjusted), 1950-2010

To help stem the productivity decline, change is needed

Characteristics of 20\textsuperscript{th} vs 21\textsuperscript{st} century clinical trials

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>20\textsuperscript{th} Century</th>
<th>21\textsuperscript{st} Century</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study design</td>
<td>Randomized, double-blind, parallel-group, placebo-controlled trial</td>
<td>Randomized, double-blind, parallel-group, placebo-controlled trial using adaptive designs</td>
</tr>
<tr>
<td>Study population</td>
<td>All comers with a given disease</td>
<td>Individuals selected based on phenotypic and genetic results</td>
</tr>
<tr>
<td>Study recruitment</td>
<td>Clinical practices</td>
<td>Global clinical trial registries and social networks organized by individuals affected by the disease</td>
</tr>
<tr>
<td>Trial visits</td>
<td>In person and audio calls</td>
<td>In person and audio and video calls</td>
</tr>
<tr>
<td>Data management</td>
<td>Paper and electronic forms</td>
<td>Electronic forms</td>
</tr>
<tr>
<td>Participant feedback</td>
<td>Limited, delayed</td>
<td>Almost universal, approximately real time</td>
</tr>
<tr>
<td>Outcome measures</td>
<td>Insensitive</td>
<td>Sensitive</td>
</tr>
<tr>
<td></td>
<td>Epidemic</td>
<td>Frequent or continuous</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>Objective</td>
</tr>
<tr>
<td></td>
<td>Provider centered</td>
<td>Patient centered</td>
</tr>
<tr>
<td></td>
<td>In clinic</td>
<td>Remote</td>
</tr>
<tr>
<td></td>
<td>Unidimensional</td>
<td>Multidimensional</td>
</tr>
</tbody>
</table>


Virtual research visits can improve efficiency of clinical trials

- **Facilitate recruitment**
  - Recruitment most common and costly cause for trial delays
  - Remote recruitment may reduce geographic barriers
  - May improve access to underserved populations with unmet therapeutic needs (e.g., nursing home patients)

- **Maximize retention**
  - Disease modifying trials in neurodegenerative disease require long duration follow up
  - Frequent in-person assessment impacts retention
  - Virtual visits may reduce burden to ongoing participation

- **Reduce variability in assessment**
  - Centralized remote raters
  - Reduce variability
  - Greater power and smaller sample size
A modified UPDRS conducted remotely is cross-sectionally and longitudinally valid

Feasibility and Value of Virtual Research Visits Using Fox Trial Finder

Methods
• Fox Trial Finder participants provided consent by phone, completed baseline surveys, downloaded video conferencing software, and received a web camera.
• After a test connection, participants underwent a remotely assessed cognition and had a virtual research visit to:
  (1) Review their history
  (2) Perform MDS-UPDRS (modified to exclude assessments of rigidity and balance)
  (3) Confirm whether PD was the most likely diagnosis
  (4) Solicit feedback on their experience

Results
• 81.4% individuals from 39 states completed the visits
• On average, participants were:
  (1) 61.6 years old
  (2) Had Parkinson disease for 8.0 years
  (3) Scored 26.5 on the Montreal Cognitive Assessment
  (4) Had modified motor score of 22.8.
  (5) Parkinson disease was most likely diagnosis in 97.0% of cases.
• Overall satisfaction with the visits was 79% (satisfied or very satisfied) among neurologists and 93% among participants.

Source: Journal of Parkinson’s Disease, 2015; 5: 505-515
In this study we connected remotely to over 160 participants in 39 states.

Map of participants

Research participants were satisfied with the virtual visits

Over 80% of participants said they would be more willing and able to participate in future research studies if they could do so remotely.
Entire clinical trials can be conducted remotely

Characteristics of select web-based clinical trials

<table>
<thead>
<tr>
<th>Source</th>
<th>Design</th>
<th>Intervention</th>
<th>No. of Participants</th>
<th>In-Person Works</th>
<th>Web-Based Recruitment</th>
<th>Web-Based Enrollment</th>
<th>Web-Based Consent</th>
<th>Web-Based Outcome Measures</th>
<th>Results Compared With Traditional Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichtenberg et al., 2004</td>
<td>Randomised, double-blind, placebo-controlled trial</td>
<td>HTN screening for vascular risk of the trial</td>
<td>355</td>
<td>No</td>
<td>Portal, opt-out advertisements</td>
<td>Portal, plus review of medical records and randomisation</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Jacobs et al., 2005</td>
<td>Randomised, double-blind, placebo-controlled trial</td>
<td>HTN care for patients with hypertension</td>
<td>391</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Portal, provison results were not used</td>
</tr>
<tr>
<td>Weizel et al., 2011</td>
<td>Open-label, multiple-center, international study</td>
<td>Lithium for amyotrophic lateral sclerosis</td>
<td>149</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Orr et al., 2014</td>
<td>Randomised, single-blind, placebo-controlled trial</td>
<td>Tolterodine tartrate extended-release formulation for overactive bladder</td>
<td>1,8</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</table>


...Or just the primary outcome

Pimavanserin for patients with Parkinson’s disease psychosis: a randomised, placebo-controlled phase 3 trial

Jeffrey Cummings, Stuart Isaacson, Roger Mills, Hilde Williams, Kathy Chi-Burr, Anne Corbett, Rahat Dhall, Clive Ballard

“The SAPS-PD (scale for assessment of positive symptoms-PD adapted) assessments were done by live video conference between the participants and a centralised, independent rater who was masked to treatment assignment.”

We are conducting a Phase III trial of isradipine in early PD at 54 sites in North America: STEADY-PD III

A Phase III, randomized, double-blind, 2-arm parallel group trial with subjects randomized 1:1 to 5mg of Isradipine IR or matching placebo twice daily for 36 months in 336 individuals with early PD

Virtual Research Visit Pilot Study—REACT-PD

- Observational study assessing feasibility of conducting virtual research visits in a subset of individuals with early PD participating in an ongoing clinical trial (STEADY-PD III)
- 40 participants in STEADY-PD III who consented to be contacted for future research will be enrolled and followed for up to 12 months
- Virtual Research visits to occur within 4 weeks after in-person clinical trial visit
- Virtual research visits will collect the same data as is collected at the corresponding in-person visit and include:

<table>
<thead>
<tr>
<th>Every Visit</th>
<th>Annual Visit Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS I-IV*</td>
<td>MDS UPDRS</td>
</tr>
<tr>
<td>Hoen and Yahr</td>
<td>MoCA</td>
</tr>
<tr>
<td>Schwab and England ADL</td>
<td>PDQ-39</td>
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<tr>
<td>C-SSRS</td>
<td></td>
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<tr>
<td>Concomitant medications</td>
<td></td>
</tr>
<tr>
<td>Evaluate need for therapy</td>
<td></td>
</tr>
<tr>
<td>Participant/investigator surveys</td>
<td></td>
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</tbody>
</table>

*Primary outcome measure of STEADY-PDIII

REACT-PD supported by:
REACT-PD Aims

1) Feasibility of remote virtual visits
2) Reliability of remote assessments of motor and non-motor function in PD compared with in-person visits
3) Value of remote research visits as measured by willingness to participate in future clinical trial visits remotely
Future directions:

**Studying the value of virtual research visits**

**Retention**
- Existing Cohort
  - STEADYPOS longitudinal follow up
  - Randomize to virtual vs in-person

**Recruitment**
- New Cohort
  - Remotely randomize to virtual vs in-person

**Outcomes**
- Recruitment
  - Proportion of participants enrolled in sub-study
- Retention
  - Annual retention rates*
  - Proportion of participants that cross over
- Power
  - Variance of outcomes conducted virtually versus in-person/mock sample size calculations
  - Ability to detect changes virtually versus remotely

*proposed primary outcome

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**Summary**

- Access to neurological care is vital but limited
- Telemedicine can improve access and outcomes in chronic neurological disorders
- Technology may be a feasible means for improving clinical trial efficiency